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the particular human nAChR studied. A rank ordering of the various agonists with each nAChR tested was obtained by qualitative comparison of the partial dose response curves for each agonist with the same receptor. The rank ordering thus lists the agonists tested in order from most potent to the least potent. Because the comparison is done with partial dose response curves rather than complete dose response curves, it is not a formal "potency study" and may more aptly be described as a "relative potency" study. These results reflect the "**relative potency**" of the various agonists.

In contrast, in the experiments described in the first Johnson DECLARATION, agonists are ranked based on the magnitude of the response determined at a single identical dose (1 μ M) of agonist. These results reflect the "**relative sensitivity**" of various agonists. Relative sensitivity refers to a listing of the agonists in order of largest normalized current magnitude to the smallest normalized current magnitude at the 1 μ M dose. Thus, in these experiments, the absolute magnitudes of currents elicited in response to a common 1 μ M-dose (i.e., relative sensitivity) of different agonists were compared, whereas the experiments described in Chavez-Noriega *et al.* present a qualitative comparison of the partial dose response curves (i.e., relative potency). The results of the relative sensitivity study revealed a difference in the relative sensitivities of human and rat $\alpha 2\beta 2$ nAChR for the four agonists studied; whereas the relative sensitivities of human and rat $\alpha 3\beta 2$ nAChR for these agonists were similar.

The results shown in both DECLARATIONS, which are designed to measure different pharmacological properties of an nAChR, demonstrate that there are significant functional and structural features of human α and β nAChR subunits and receptors formed therefrom, which cannot be predicted based on the properties of nAChR subunits or receptors from other species of animal.

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Consideration of the above remarks, and allowance of the application are respectfully requested.

Respectfully submitted,
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